

Amendment and Reply Under 37 C.F.R. § 1.111  
U.S. Application Serial Number 09/691,504

of the comments below.

Claims 18, 55 and 78 have been amended to more clearly describe the claimed invention. Claims 56-59 have been amended to claim proper dependency and more clearly describe the claimed invention. No new matter has been added by the claim amendments. Claims 18-23, 26, 29-38, 55-64, 67, 70-96, 99, and 102-107 are pending.

**CLAIM REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

Claims 18-23, 26, 29-38, 55-64, 67, 70-96, 99, and 102-107 have been rejected as not being adequately described in the specification. The Examiner states that the specification only discloses the use of dendritic cells or monocytes and does not provide adequate description of all antigen presenting cell for use in the present invention.

In view of the amendments of said claims as set forth above, withdrawal and reconsideration of this rejection is respectfully requested. The specification clearly defines antigen presenting cells as specialized lymphoid cells such as dendritic cells, B cells, and monocytic cells, which are capable of inducing T-cell activation. (*See* pages 9, 26 and 64 of the specification). This description is adequate to describe the invention and enable a person of skill in the art to make and use the claimed invention. However, claims 18, 55 and 78 have been amended to recite “which are capable of inducing T cell activation” to more specifically and clearly define “antigen presenting cells” as they are disclosed in the specification. Accordingly, withdrawal and reconsideration of this rejection is respectfully requested.

The Examiner also states that the specification only discloses treatment using autologous and syngeneic cells and does not provide adequate description of treatment using xenogeneic or allogeneic cells. Applicants respectfully traverse this rejection.

Claims 18, 55 and 78 have been amended to recite “which are autologous or allogeneic” to more specifically define the antigen presenting cells. The specification

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provides examples demonstrating the use of allogeneic APCs. For example, the application describes one embodiment of the present invention where the antigen presenting cells are obtained from an HLA-matched donor. (*See* page 13 of the specification). APCs from a HLA-matched donor are allogeneic. The specification provides adequate disclosure to enable a person of skill in the art to practice the claimed invention with antigen presenting cells regardless of the source, including, for example, allogeneic cells from a HLA-matching donor. Furthermore, the specification provides, as Example 1, a murine model in which allogeneic dendritic cells and spleen cells are used according to the present invention. (*See* page 19). Thus, the specification clearly provides exemplification of the use of allogeneic cells in the present invention and reconsideration and withdrawal of this rejection are therefore respectfully requested.

Further, the Examiner asserts that the specification does not teach tumor cells with express "shared" tumor antigens and, therefore, the specification provides insufficient guidance to enable treatment of tumors pulsed with tumor lysates from a tumor which "does not express any of the same tumor antigens as the host tumor."

Applicants respectfully submit that this misapprehends the invention. Applicants provide guidance on generating immune response against shared tumor antigens. The specification provides examples of shared tumor antigens, such as those from the MAGE gene family, which is the best characterized example of a type of tumor antigen that is shared by different tumors. (*See* pages 11 and 30). Pardoll *et al.* disclose that the MAGE family of antigens are expressed in melanoma and in other tumor types. For example, the specification discloses an example where MAGE-1 or MAGE-3 antigens were used to develop a composition according to the present invention. (*See* page 30). Applicants respectfully submit that this rejection should be withdrawn.

Finally, the Examiner asserts that the specification does not enable administering the

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disclosed immunogenic compositions by any route of administration to any site in the mammal to be treated.

Applicants respectfully disagree and submit that the application enables one skilled in the art to administer the composition of the present invention by any route of administration to any site in the mammal to be treated. The specification indicates that the vaccine composition of the present application could be administered continuously (*e.g.*, by IV drip), intramuscularly, transdermally, using sustained release delivery, and preferably intradermally or subcutaneously. (*See* specification at page 17). At the time of the present invention, one skilled in the art would have had knowledge of various sites and modes available for administering a vaccine to determine, based on the circumstances, a suitable mode or route of administration for the vaccine in a particular individual. The Examiner relies on an article by Nestle *et al.* in which the author stated that his vaccine should be injected near to or into a professional lymphoid organ. The present invention is not limited to one route of administration based on another researcher's (*i.e.*, Nestle's) decision to inject directly into a lymph node. This is particularly true when one considers that Nestle's decision was based on speculation that injecting DCs in peripheral tissue “*may* lead to a substantial loss of DCs during migration into spleen or lymph node.” (Nestle *et al.* at 328)(emphasis added). The present invention can be administered by any mode of administration, and Applicants respectfully request withdrawal and reconsideration of this rejection..

**CLAIM REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

Claims 56-59 and 80-81 have been rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which is regarded as the invention. The Examiner states that the term "about" is indefinite as it is a relative term with no fixed metes and bounds.

Applicants respectfully traverse and submit that the rejected claims are definite.

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Applicants submit that a person of skill in the art would know the metes and bounds of the claims, which are made clear from the specification. Claims 56-59 and 80-81 provide ranges of plaque forming units (PFU) or antigen presenting cells. One of skill in the art would understand from the nature of the claimed subject matter that the ranges, which are disclosed in the specification, encompass cell counts and plaque forming units that are not precisely, for example, ten thousand PFU to ten million PFU. Rather, one skilled in the art would know the metes and bounds of “about” as it applies to the claimed subject matter. In *Eiselstein v. Frank*, 52 F.3d 1035, 34 USPQ2d 1467 (Fed. Cir. 1995), the Federal Circuit held that “[t]he meaning of the word 'about' is dependent on the facts of a case, the nature of the invention, and the knowledge imparted by the totality of the earlier disclosure to those skilled in the art.” Applicants, therefore assert that one skilled in the art would clearly understand, in view of the state of the technology embodied in the invention, a reasonable meaning of “about” in the particular circumstances. Applicants respectfully urge that this rejection should also be withdrawn.

**CLAIM REJECTIONS UNDER 35 U.S.C. § 103(a)**

Claims 18-23, 26, 29-38, 55-64, 67, 70-96, 99, and 102-107 have been rejected as being unpatentable over Nestle et al. (“Nestle”) in view of Sivandandham *et al.* (“Sivandandham”). The Examiner states that Nestle teaches methods of vaccinating patients with patient-derived dendritic cells pulsed with melanoma tumor lysate.

Applicants respectfully traverse. The rejected claims are directed to immunotherapeutic vaccines and methods of using vaccines that have two parts. In the present invention, the vaccine is comprised of i) a recombinant vaccinia virus (VVR) encoding at least one first immunostimulating molecule, and ii) antigen presenting cells pulsed with a preparation comprising enucleated cytosol and cell membranes of cancer cells infected with VVR encoding at least one second immunostimulating molecule. The antigen presenting cells are pulsed with tumor cells infected with VVR to allow for the production of

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enhanced immune response.

In contrast, Nestle, the primary reference relied on by the examiner, does not teach or suggest a vaccine comprising two parts. Instead, Nestle only teaches a vaccine comprising of dendritic cells pulsed with either peptides or tumor lysates. Nestle does not disclose or suggest the use of VVR encoding immunostimulating molecules, let alone the use of VVR in conjunction with antigen presenting cells pulsed with tumor cell lysates of cancer cells infected with a VVR encoding a second immunostimulating molecule for use as anti-tumor therapies. Therefore, the primary reference fails to teach or suggest a vaccine comprised of two parts. Sivanandham *et al.* does not cure the deficiencies of Nestle. Sivanandham *et al.* discloses a murine colon oncolysate prepared with IL-2 encoded VVR used in treating syngeneic murine colon adenocarcinoma metastasis. It does not disclose a two- part vaccine of the present invention. Therefore, the combination of art relied on by the examiner in rejecting the above-mentioned claims fails to teach or suggest the claimed invention and, therefore, cannot render it obvious. Applicants respectfully urge that this rejection should also be withdrawn.

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## CONCLUSION

In view of the foregoing amendments and remarks, it is firmly believed that the subject invention is in condition for allowance, which action is earnestly solicited.

The Office is hereby authorized to charge Deposit Account No. 11-0600 with any additional fees required by this paper or credit any overpayment.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned directly at (202) 220-4258.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

Date: 4-17-03

  
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Marked Up Version To Show Changes Made

18. (First Amended) An immunotherapeutic vaccine comprising:
  - (a) a first part comprising a first recombinant vaccinia virus encoding at least one first immunostimulating molecule; and
  - (b) a second part comprising antigen presenting cell, which are capable of inducing T-cell activation and which are autologous, syngeneic or allogeneic, pulsed with a preparation comprising enucleated cytosol and cell membranes of cancer cells infected with a recombinant vaccinia virus encoding at least one second immunostimulating molecule.
55. (First Amended) A method for eliciting an anti-cancer immune response in a subject, which comprises:
  - (a) administering a first recombinant vaccinia virus encoding at least one first immunostimulating molecule; and
  - (b) administering a composition comprising antigen presenting cells, which are capable of inducing T cell activation and which are autologous, syngeneic or allogeneic, pulsed with a preparation comprising enucleated cytosol and cell membranes of cancer cells infected with a second recombinant vaccinia virus encoding at least one second immunostimulating molecule.
56. (First Amended) The method of claim [56] 55, wherein about 10<sup>4</sup> to about 10<sup>8</sup> PFU of the first recombinant vaccinia virus is provided [the amount of the first recombinant vaccinia virus is from about 10<sup>4</sup> to about 10<sup>8</sup> PFU].
57. (First Amended) The method of claim [56]55, wherein [the amount of the first recombinant vaccinia virus is] about 10<sup>7</sup> PFU of the first recombinant vaccinia virus is provided.
58. (First Amended) The method of claim [56]55, wherein [the number of antigen presenting cells is from] about 10<sup>5</sup> to about 10<sup>7</sup> antigen presenting cells are provided.
59. (First Amended) The method of claim [56]55, wherein [the number of antigen presenting cells is from] about 10<sup>6</sup> to about 5x10<sup>6</sup> antigen presenting cells are provided.
78. (First Amended) A method of treating cancer in a subject, which comprises:
  - (a) administering a first live recombinant vaccinia virus encoding at least one first immunostimulating molecule; and
  - (b) administering an effective amount of a composition comprising antigen

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presenting cells, which are capable of inducing T-cell activation and which are autologous, syngeneic or allogeneic, pulsed with a preparation comprising enucleated cytosol and cell membranes of cancer cells infected with a second recombinant vaccinia virus encoding for at least one second immunostimulating molecule.